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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,338	06/18/2001	Sohei Kanno	209861US0PCT	8914

38108 7590 01/14/2004

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,338	KANNO ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 9-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5/1/04 9/24/04
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Amendment filed 13/3/03 has been entered.

Election/Restriction

2. Applicant's election with traverse of Group II (Claims 5-8), on 11/3/03, is acknowledged. The traversal is on the ground(s) that it would not be a serious burden to examine groups I-III, together. This is not found persuasive because a search of groups I-III would not be co-extensive particularly with regard to the literature search. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 5 recites a protein, claims 6-8 recite a DNA but said claims do not recite that they are isolated or purified. The claims as currently recited encompass these naturally-occurring compounds. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man,

and as such is non-statutory subject matter. It is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

Claim Rejection, 35 U.S.C. 112

4. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because "stringent" hybridization conditions are not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the claimed polynucleotide the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claim 8 is indefinite because "stringent" hybridization conditions have been partially. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the claimed polynucleotide the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claims 5-7 are ambiguous because they recite subsections (C) and (D) but do not include subsections (A) and (B). It is suggested subsections (C) and (D) be amended to subsections (A) and (B) to overcome the rejection.

5. ***Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph***

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

A “specific utility” is a utility that is specific to the subject matter claimed, as opposed to a “general utility” that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied

by the specifications disclosure of the properties of a material, alone or taken with

the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed DNA and protein of claims 5-8. For example, the specification states that the claimed invention is, "a novel ABC transporter and gene coding for a protein that is a constituent of the ABC transporter and the gene can be utilized for breeding of microorganisms showing modified transport of amino acids across a cell membrane and so forth". Based on the record, there is not a "well established utility" for claimed ABC transporter because the amino acids transported have not been disclosed and ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters with diverse effects (see IDS ref AAA). The utilities asserted by Applicant are not specific or substantial. Neither the specification nor the art of record disclose the protein of SEQ ID NO:9 encoded by the DNA of SEQ ID NO:7 or fragments thereof useful to identify drugs that affect said protein and modulate a specific ABC transporter activity. Similarly, neither the specification nor the art of record disclose any instances where disorders or disease occur are a result of dysfunctional or functional protein of SEQ ID NO:9, or such disorders or functions can be effected by interfering with claimed ABC transporter. There is no disclosure of the beneficial affects of claimed transporter in bacteria which can be utilized for

breeding. Thus the corresponding asserted utilities for the ABC transporter, with no disclosed ligands or compounds which it transports, are essentially methods of treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the ABC protein/DNA and fragments thereof, further experimentation is necessary to attribute a utility to the claimed invention. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

The specification discloses the claimed ABC protein/DNA is related to other proteins of the ABC transporter family. Applicant has used the homology to form the basis for utility for the claimed ABC protein/DNA. There is no disclosure in the art that proteins which have the homology disclosed in the specification are "sufficiently similar" and have the same function or transport the same compounds. It is unlikely, based on the art and Applicants specification that the ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters with diverse effects. Therefore, the first question

is, to which family of proteins does ABC belong, and secondly which particular member of the family has the same identical activities, functions and pharmacological of the ABC transporter of SEQ ID NO:9. The specification provides no clear answers. There is no disclosure of when a protein is considered "sufficiently similar" to be considered having all the properties of a family or of a specific species. There is no disclose in the specification of the percent identity to related family members to assign functionality. Applicant has made sequence related predictions based on a limited homology between proteins, and based utility arguments on the family of proteins that have shown the closest identity. Based on the diversity of activity, functionality and ligand specificity of the ABC transporter family further experimentation is required to attach a specific function to the claimed ABC transporter. The specification does not disclose the specific function of the claimed ABC transporter, the transporter mechanism involved in movement of molecules across cell membranes, and the cytotoxic agents or ions that are moved. There is no disclosure by which claimed ABC transporter function, the utility in testing for its ability to confer drug resistance on cells expressing ABC (either normally or artificially), is based, or what specific drugs or ligands effect what specific transport, in cells expressing ABC, which in turn leads to utility in breeding. There is no disclosure of the scientific reasoning, that sequence similarity, in instant case, between claimed ABC transporter and other proteins that can be used to selectively predict a specific function, dysfunction, and activity of the ABC transporter family. Further

the utility of claimed ABC, as postulated by applicant, consist of its potential role as an object of "use-testing".

Therefore the claimed ABC protein/DNA, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed polypeptide/DNA. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed protein/polynucleotide was, as of the filing date, useful for diagnosis, prevention and treatment of an disease, or for screening compounds. Until some actual and specific significance can be attributed to the claimed ABC protein/DNA, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The ABC protein/DNA may share some structural similarity to the ABC transporter family based on undisclosed sequence similarity. As disclosed by the ABC transporter family may have diverse effects, and play roles in the pathogenesis of various diseases. Although the family ABC transporter proteins may share some common structural motifs to claimed ABC protein/DNA, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for claimed invention or molecules transported, or the biological significance of the claimed ABC protein/DNA, there is no immediately evident patentable use. To employ the protein/DNA of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real

world" use for claimed polypeptide, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful. Further there is no disclosure of what is the critical structure of the invention that is required for functionality.

The claimed ABC protein/DNA belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

The diversity of the family of proteins, to which claimed ABC transporter is suggested to belong, has already been described. Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. Without knowing a biological significance of the claimed polypeptide/DNA, one of

ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by the ABC transporter family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The utility must be specific, substantial. The assertion that the claimed invention has utility in drug screening, testing, drug development and disease diagnosis, do not meet the standards for a specific, substantial, or well-established utility for reasons set forth above.

The specification does not disclose the significance of any test results, nor is there any evidence that the significance was known as of the filing date. If the expression of the claimed polypeptide/DNA increases, is this a positive or negative outcome? Would this be a toxic response or not? The disclosure is insufficient to evaluate the results of the test in any meaningful manner.

None of the utilities identified by Applicant, have been demonstrated to be specific to claimed ABC transporter. One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed

species based on the knowledge of the class. However, no practical benefit has been shown for the use of ABC2. The requirement in any particular case, however, is that practical utility can be inferred if each and every member of the broad class possesses a common utility.

Applicant has failed with respect to claimed ABC transporter, have not described the family or the compounds in enough detail to show, by a preponderance of the evidence, that claimed ABC transporter has any substantial use. The record shows that the ABC transporter family is diverse, and has such a broad definition, that a "common utility" cannot be defined. Moreover, the evidence of record is inadequate to determine the disease(s), drug(s) or toxicological screen(s) for which the compounds would be useful. In *Brenner,* the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible tumor-inhibiting effects and an adjacent homologue of the compound had proven effective. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. The question at issue is whether or not the broad general assertion that the claimed ABC polypeptide/DNA might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board

of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

However, for reasons set forth above, Applicant has not presented sufficient evidence to support specific utility for ABC transporter or its variants. The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

6. Claims 5-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed polypeptide of SEQ ID NO:9 encoded by the polynucleotide of SEQ ID NO:7. The claims encompass polypeptides and polynucleotides and variants thereof which may be completely unrelated to the protein of SEQ ID NO:9 or DNA of SEQ ID NO:7, structurally and functionally, further even lacking the critical feature of the invention. Further experimentation is necessary to attribute a utility to the claimed nucleic acid/protein and variants thereof. Therefore claims 5-8 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The claims fail to disclose how to use the claimed invention for the reasons given above (lack of utility). Further the claims are drawn to an orphan ABC transporter protein/DNA. The claimed nucleic acid encodes an orphan ABC transporter whose activity, compound transported, activating ligands and functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed ABC transporter. There is no disclosure of the specific compounds that are transported, proteins activated in the signal transduction pathway or what ligand is capable of binding to the polypeptide encoded by the claimed polynucleotide,

so as to disclose a specific function for the claimed polynucleotide. Therefore nucleic acid encoding unrelated and inactive proteins is encompassed by the claims. The specification does not disclose how to produce active variants or how to use inactive ones. Substitutions, deletions, insertions, additions or inversions that result in active variants are not disclosed. Substitutions, deletions, insertions, additions or inversions that are detrimental to transporter variant activity are not disclosed. There is no disclosure of how to assay variants since compound transported, natural ligand and function of the claimed invention is unknown.

The complex nature of ion transporters and the unpredictability of assigning a function to claimed transporter function with no known ligand, compound transported, or function is described in the rejection under 35 USC § 101 and 35 USC § 112, 1st paragraph..

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, many of the polypeptides, encoded by the nucleic acids which hybridize to the polynucleotide of SEQ ID NO:7, may be inactive or unrelated to the nucleic acid encoding the polypeptide of SEQ ID NO:9. The specification does not disclose how to produce active variants. The specification does not disclose a utility for or how to use said inactive or unrelated polypeptides encoded by claimed nucleic acid molecule. The claimed nucleic acid encodes an

ABC transporter whose activity, compound transported, activating ligands, functionality have not been disclosed. Neither the claims nor the specification disclose what specific biological activity is associated with the claimed transporter. There is no disclosure of how to assay variants identified by the hybridization procedure since the ligand, compound transported and function of the claimed invention is unknown. Specific hybridization conditions have not been provided. Therefore the hybridization conditions recited in the claim do not constitute a meaningful structural limitation.

Pertaining to claims 7 and 8, instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence

does not support claims to any nucleic acid hybridizing to same, given the lack of guidance regarding what sequences would hybridize specifically to sequence complementary to the polynucleotide of SEQ ID NO:17and not other, related sequences. Further, many of the polypeptides encoded by the nucleic acids isolated by hybridization will be unrelated to the protein of instant invention, being devoid of its characteristic structural and functional features. Said unrelated polypeptides may be produced by frame shift in the coding sequence of the nucleotide, for example. Other polypeptides may be truncated, for example. Due to the large quantity of experimentation necessary to identify the polypeptides with the structural and functional features of instant invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:9 are also encompassed by the claim), and the breadth of the claim which fail to recite meaningful structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

The specification discloses a polynucleotide which encodes claimed transporter. The specification does not teach how to make functional claimed transporter variants or to use inactive variants. The prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered, nor does the specification provide any

guidance as to how the skilled artisan could use inactive claimed ABC transporter variants. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that claimed ABC transporter variants could be used for any purpose. Further the nucleic acids that comprise variants of SEQ ID NO:7 or encode variants of the polypeptide of SEQ ID NO:9 may not specifically hybridize to the polynucleotide of SEQ ID NO:7 or to the polynucleotide that encodes the polypeptide of SEQ ID NO:9. Applicant has not disclosed how to use said nucleic acids that do not specifically hybridize the polynucleotide of SEQ ID NO:7 or to the polynucleotide that encodes the polypeptide of SEQ ID NO:9. Therefore, pertaining to claimed variants, due to the large quantity of experimentation necessary to identify the nucleic acids encoding polypeptides with the structural and functional features of instant ABC transporter (the critical feature of the invention is not disclosed, i.e. structure and function relationship), the lack of direction/guidance presented in the specification regarding the identification, purification, isolation, characterization and assaying (no specific assay disclosed which measures claimed transporter activity) of claimed invention, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:9 are also encompassed by the claim), construction of active variants (no disclosure of which amino acids can be mutated and still provide active protein) and the breadth of the claim which fail to disclose the compound transported and functional limitations containing critical feature of the invention, undue experimentation would be

required of the skilled artisan to make or use the claimed invention in its full scope. For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by the skilled artisan to use the instant invention.

Claim Rejection 35 USC § 112, 1st paragraph (Written Description)

7. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are claims 5-8 are directed to:

i) a protein which has the amino acid sequence of SEQ ID NO:9 including substations, deletions, addition or inversion of one or several amino acids and has ATPase activity.

ii) DNA encoding the protein of i).

iii) DNA which hybridizes to a polynucleotide with the nucleotides sequence 1117-1752 of SEQ ID NO:7 or a probe prepared from said nucleotide sequence

The claims encompasses variants of the nucleic acid molecules of SEQ ID NO:7 encoding variants of the protein disclosed in SEQ ID NO:9, said variants may be completely unrelated, structurally and functionally to the protein encoded by SEQ ID NO:9 .

The common function of the nucleic acid (SEQ ID NO:7) encoding the polypeptide (SEQ ID NO:9), which is based upon a common property or critical technical feature of the genus claimed is not disclosed. The claims, as written, encompass nucleic acid encoding polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NO:7 encoding the polypeptide of SEQ ID NO:7 does not adequately describe the scope of the use of the claimed genus, which encompasses a substantial variety of subgenera including polynucleotides, proteins, variants of said polynucleotides and proteins, allelic variants, chimeric constructs, fusion constructs, variants and polynucleotides which hybridize to the nucleic acid of SEQ ID NO:7, which may encode polypeptides completely, unrelated functionally to the polypeptide of SEQ ID NO:9. A description of a genus of

polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. For example, what regions and fragments of the claimed VR-L contain a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, and hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and proteins encompassed. No identifying characteristic or property of the instant polypeptides/polynucleotide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of

the genus, and because the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, **there is no clear evidence of activity possessed by the claimed genus of nucleic acid molecules encoding variant ABC transporter polypeptides, the critical special technical feature of the polypeptides or how the critical special technical feature encompassed by the genus claimed relates to function.** Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the claimed variants have the same activity as the protein disclosed in SEQ ID NO:9, since no activity is disclosed, or if they contain the domain(s) of SEQ ID NO:9, containing the critical special technical feature of the claimed transporter, since no critical special technical feature is disclosed. The specification does not disclose which amino acids encode the ATPase activity, and how structure is related to function.

Pertaining to variants to the nucleic acid/protein the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fibers v. Revel*, 25 USPQ d. 1601 at 1606 (CAFC 1993) and *Amen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a

genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Therefore the specification fails to disclose the activity of the claimed genus of polypeptides/polynucleotides, the critical special technical feature of the polypeptides/polynucleotides or how the critical special technical feature encompassed by the fragments and variants of claimed ABC transporter relates to function. Similarly pertaining to nucleic acids which hybridize to the polynucleotide of SEQ ID NO:7, under unclearly defined hybridization conditions, what is the special technical feature encompassed by said nucleic acids and how do they relate to function.

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein/nucleic acid disclosed in SEQ ID NO:9 and 7, respectively. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of nucleic acids/polypeptides . There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no disclosure of the specific activity of claimed ABC

transporter and how it is specifically assayed. The specification nor claims disclose the specific activity of the claimed ABC transporter of instant invention nor a description of the conserved regions which are critical to the structure and function of the genus claimed.

There is no disclosure of the compound transported by the claimed genus nucleic acids encoding a claimed ABC transporter or the nature of the signal or specific signal transduction pathway. The claimed nucleic acid encodes an orphan ABC transporter whose activity, associated function and activating ligands have not been disclosed. The neither specification nor prior art provide a specific assay for the genus claimed. Nucleic acids/proteins comprising variants of claimed ABC transporter may be completely unrelated to the protein encoded by the nucleic acid of SEQ ID NO:7 The superfamily of ion transporters are specialized proteins designed for chemical recognition of ligands, transport of specific compounds, and subsequent transduction of information encoded in those ligands/compounds to the machinery of the cell. Ion transporters interact with many diverse compounds having diverse effects. The important features which would help to define the claimed ABC transporter activity and define the genus claimed have not been disclosed in the specification nor prior art. Further the activity transduced is not disclosed or how it relates structure to function. Similarly, pertaining to nucleic acids which hybridize to the polynucleotide of SEQ ID NO:7, under unclearly defined hybridization conditions, what is the special technical feature encompassed by said nucleic acids and how do they relate to function.

The claims encompass nucleic acids encoding proteins which are structurally and functionally unrelated to the protein of SEQ ID NO:9. Therefore instant specification fails to provide sufficient descriptive information, such as definitive structural/ functional features of the claimed genus of polypeptides/polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The neither specification nor claims disclose the specific activity of the "orphan claimed ABC transporter " of instant invention, how it is assayed, nor a description of the conserved regions which are critical to the structure and function of the genus claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 703-308-9435. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Nirmal S. Basi
Art Unit 1646

Michael D. PAK
MICHAEL PAK
PRIMARY EXAMINER

1/12/03